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— *as to the applicant's entitlement to claim the priority of the
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*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: SUBSTITUTED IMIDAZOLES AS DUAL HISTAMINE H₁ AND H₃ AGONISTS OR ANTAGONISTS

(57) Abstract: The present invention discloses novel substituted imidazole compounds which have H₃ receptor antagonist or dual histamine-H₁ and H₃ receptor antagonist activity as well as methods for preparing such compounds. In another embodiment, the invention discloses pharmaceutical compositions comprising such imidazoles as well as methods of using them to treat allergy, nasal congestion, inflammatory and CNS-related diseases and others.



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INTERNATIONAL SEARCH REPORT

International Application No.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D403/06 C07D401/14 C07D401/06 C07D401/12 A61P29/00
 A61P37/00 A61K31/415 A61K31/44 C07D233/54 C07D213/38
 //(C07D403/06,233:00,207:00),(C07D401/14,233:00,213:00,211:00),

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>CHEMICAL ABSTRACTS, vol. 121, no. 7, 1994 Columbus, Ohio, US; abstract no. 83338, GIZOR ET AL: "Process for production of new 4-methyl-2-imidazolinone derivatives for treatment of cerebrovascular diseases and hypoxia and pharmaceutical preparations containing them" XP002205148 abstract & HU 213 104 B (RICHTER GEDEON VEGYESZET) 28 February 1997 (1997-02-28) page 4, column 1, line 21 - line 22 --- -/---</p>	1,4

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

19 July 2002

Date of mailing of the international search report

02/08/2002

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/29062

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 (C07D401/06,233:00,211:00),(C07D401/12,233:00,213:00)

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	HULS A ET AL: "Diphenylmethyl ethers: synthesis and histamine H3-receptor antagonist in vitro and in vivo activity" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 6, no. 16, 20 August 1996 (1996-08-20), pages 2013-2018, XP004135646 ISSN: 0960-894X page 2016, final sentence examples 3A-3F	1,14
Y	WO 00 23438 A (SCHERING CORP) 27 April 2000 (2000-04-27) examples 4,7,17-20 ----- -/--	1,14

☒ Further documents are listed in the continuation of box C.

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L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

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European Patent Office, P.B. 5818 Patentlaan 2
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Bakboord, J

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/29062

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 182 294 A (MOERSDORF PETER ET AL) 26 January 1993 (1993-01-26) column 2, line 37; claim 1 ----	1, 14
Y	EP 0 289 227 A (SYNTEX PHARMA LTD) 2 November 1988 (1988-11-02) claims 1, 11 ----	1, 14
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Y	BUSCHAUER A: "IMIDAZOLYLALKYLGUANIDINE MIT DIARYL-PARTIALSTRUKTUREN IMIDAZOLYLALKYLGUANIDINES WITH DIARYL STRUCTURAL PARTS" SCIENTIA PHARMACEUTICA, OESTERREICHISCHE APOTHEKER VERLAGSGESELLSCHAFT, AT, vol. 56, no. 2, 1988, pages 81-88, XP001062163 ISSN: 0036-8709 examples 14A, 14B ----	1, 14
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A	WALCZYNSKI: "non-imidazole histamine H3 ligands. Part I. Synthesis of 2-(1-piperaziny1)-and 2-(hexahydro-1H-1,4-diazepin-1-yl)benzothiazole derivatives as H3-antagonists with H1 blocking activities" IL FARMACO, vol. 54, 1999, pages 684-694, XP002204857 NL cited in the application the whole document -----	17

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US 01/29062

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 13 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.
2. ☒ Claims Nos.: 1-15 part
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 01 /29062

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-15 part

Present claims 1 (and dependent claims 2,3,5,8,9), 10, 11 (and dependent claim 12), 13, 14, and 15 relate to compounds of formula I in which formula II is a piperidine derivative and formula III is a cyclohexane derivate. Claim 4 (and dependent claim 6) relate to a compound of formula I in which formula II is a piperidine derivative in which one of the CH₂ groups is replaced by a group Z.

It appears however from the description of the present application that all worked examples concern compounds of formula I wherein formula II is a piperazine derivative and formula III is a piperidine derivative. This contradiction between claims and description renders the scope of the claims unclear within the meaning of Article 6 PCT. Consequently, the search has been limited to compounds of formula I wherein formula II is a piperazine derivative and formula III is a piperidine derivative.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/29062

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INTERNATIONAL SEARCH REPORT

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International Application No

PCT/US 01/29062

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